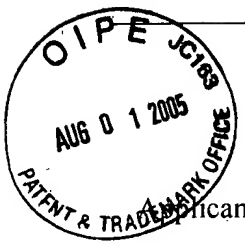
AFW

Docket No.: VANM212.001AUS **Customer No. 20,995**



PETITION

Applicant	:	Remacle et al.
App. No	:	09/816,763
Filed	:	March 23, 2001
For	:	METHOD AND KIT FOR THE SCREENING, THE DETECTION AND/OR THE QUANTIFICATION OF TRANSCRIPTIONAL FACTORS
Examiner	:	Kim, Young J.
Art Unit	:	1637

PETITION UNDER 37 CFR 1.181(a) TO WITHDRAW HOLDING OF ABANDONMENT BASED ON EVIDENCE THAT A REPLY WAS TIMELY MAILED OR FILED

Mail Stop: Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

We are in receipt of a Notice of Abandonment for the above-identified application, which was mailed on July 13, 2005.

We request withdrawing holding of Abandonment since we timely filed a response to the January 7, 2005 Office Action before the three-month extension of time date on July 6, 2005.

Enclosed is a copy of the PTO stamped postcard and response filed on July 6, 2005 and date-stamped on July 8, 2005.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 28, 2005

By: _____

Marina L. Gordey
Registration No. 52,950
Agent of Record
Customer No. 20,995
(805) 547-5580

1831641:vr
072605

Please Direct All Correspondence to Customer Number **20995**

PETITION TRANSMITTAL LETTER

Applicant	:	Remacle et al.
App. No	:	09/816,763
Filed	:	March 23, 2001
For	:	METHOD AND KIT FOR THE SCREENING, THE DETECTION AND/OR THE QUANTIFICATION OF TRANSCRIPTIONAL FACTORS
Examiner	:	Kim, Young J.
Art Unit	:	1637

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Mail Stop: Petitions, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

July 28, 2005
(Date)

Marina L. Gordey, Reg. No. 52,950

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application are:

(X) Petition under 37 CFR 1.181(a) to Withdraw Holding of Abandonment Based on Evidence that a Reply was Timely Mailed or Filed.

(X) Copy of PTO stamped postcard and response filed July 6, 2005.

(X) The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 11-1410.

(X) Return prepaid postcard.

Marina L. Gordey
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1831664:vr
072605

UTILITY/DESIGN PATENT
(amend/final ~~amend/appeal~~)

Date: 7/6/05
Date of Action: 1/7/05

Rec'd in the USPTO on the date stamped hereon via Certificate of Mail:
Docket #: VAnm212.001AUS Applicant: Remacle, et al
Title: Method and Kit for the Screening the Detection...
App No.: 09/816,763 Filed: 3/23/01
VERIFIED BY: Asst: DMB Atty: DoH QC: DoH / SC

- ☒ Transmittal Letter
- ☒ Amendment in 11 pgs
- ☐ ____ Month Extension Requested
- ☐ Information Disclosure Statement; with PTO-1449 w/_____ Ref(s)
- ☐ Terminal Disclaimer in ____ pgs
- ☐ Sequence Submission Statement
- ☐ Sequence Listing in ____ pgs
- ☐ ____ copies of CRF Containing Seq List
- ☐ _____
- ☒ Return Prepaid Postcard
- ☐ Req for Drawing Changes/Corrections
- ☐ ____ sheets of RED-Lined Drawings
- ☐ Notice of Appeal in Duplicate
- ☐ Appeal Brief in ____ pgs in Triplicate
- ☐ Request for Oral Hearing
- ☒ $ 510 Check for Filing Fees
- ☐ _____
- ☐ _____
- ☐ _____
- ☐ _____

(7/14/03)

Knobbe, Martens, Olson & Bear LLP
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INTELLECTUAL PROPERTY LAW
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Irvine, CA 92614

Please Direct All Correspondence to Customer Number **20995**

AMENDMENT / RESPONSE TRANSMITTAL

Applicant	:	Remacle, et al.
App. No	:	09/816,763
Filed	:	March 23, 2001
For	:	METHOD AND KIT FOR THE SCREENING, THE DETECTION AND/OR THE QUANTIFICATION OF TRANSCRIPTIONAL FACTORS
Examiner	:	Kim, Young J.
Art Unit	:	1637

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

July 6, 2005
(Date)

Daniel Hart, Reg. No. 40,637

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted herewith for filing in the above-identified application are the following enclosures:

(X) Amendment and Response to Office Action in 11 pages.

The fee has been calculated as shown below:

The present application qualifies for Small Entity Status under 37 CFR 1.27.

FEE CALCULATION				
FEE TYPE		**FEE CODE**	**CALCULATION**	**TOTAL**
3 Month Extension	*1.17(a)(3)*	2253 ($510)		$510
			TOTAL FEE DUE	$510

(X) An extension of time is hereby requested by payment of the appropriate fee indicated above.

(X) A check in the amount of $510 is enclosed.

07/11/2005 GWORDOF1 00000025 09816763
01 FC:2253 510.00 OP

Please Direct All Correspondence to Customer Number **20995**

(X) Return prepaid postcard.

(X) Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Daniel Hart
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Customer No. 20,995
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1799411:dmb
070105

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Remacle et al.
Appl. No.	:	09/816,763
Filed	:	March 23, 2001
For	:	METHOD AND KIT FOR THE SCREENING, THE DETECTION AND/OR THE QUANTIFICATION OF TRANSCRIPTIONAL FACTORS
Examiner	:	Kim, Young J.
Group Art Unit	:	1637

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

July 6, 2005
(Date)

Daniel Hart

Daniel Hart, Reg. No. 40,637

AMENDMENT AND RESPONSE TO OFFICE ACTION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action mailed January 7, 2005, please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 6 of this paper.

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A screening and/or quantification method of one or more transcriptional factors(s) present in a cell or cell lysate, said method comprising the steps of:

~~a.~~ (a) binding to an insoluble solid support double-stranded DNA sequence(s) at the concentration of at least 0.01 pmole/cm^2 of said solid support surface, wherein the solid support is an array bearing at least 4 spots/cm^2 of solid support surface, each spot containing double-stranded DNA sequence(s) for the binding of transcriptional factor(s), said double-stranded DNA sequence comprising a specific sequence, said specific sequence being able to bind said one or more transcriptional factor(s) and said double-stranded DNA sequence being connected to the surface of the solid support by a spacer wherein said spacer is ~~corresponding to or comprising at least~~ a double-stranded DNA nucleotide sequence of between about 50 and about 250 base pairs, or wherein the spacer comprises a double-stranded DNA nucleotide sequence of between about 50 and about 250 base pairs;

~~b.~~ (b) putting into contact said one or more transcriptional factor(s) with said bound double-stranded DNA sequence(s); and

~~c.~~ (c) identifying and/or quantifying a signal resulting from the binding of said transcriptional factor(s) upon said double-stranded DNA sequence(s).

2. **(Original)** The method according to claim 1, wherein the transcriptional factor is present in solution at concentration lower than 20 nmolar (nM).

3. **Canceled**

4. **(Currently amended)** The method according to claim 1, wherein the signal resulting from the binding of the transcriptional factor upon the double-stranded DNA sequence is a non-radioactive ~~resulting~~ signal.

5. **(Previously presented)** The method according to claim 1, wherein the signal resulting from the binding of the transcriptional factor upon the double-stranded DNA sequence is obtained through an enzymatic reaction.

6. **(Previously presented)** The method according to claim 1, for the screening and/or quantification of multiple different transcriptional factors present in a same biological sample.

7. **(Previously presented)** The method according to claim 1, for the screening and/or quantification of transcriptional factors selected from the group consisting of NF-KB, AP-1, CREB, SP-1, C/EBP, GR, HIF-1, Myc, NF-AT, Oct, TBP, CBF-1 and factors listed in table 1.

8. **(Previously presented)** The method according to claim 1, for the screening and/or quantification of multiple different transcriptional factors upon a same support upon the same multiwell plate.

9-11. **Cancelled**

12. **(Previously presented)** The method according to claim 1, wherein the binding of the double-stranded DNA sequence(s) to the insoluble solid support is of non-covalent type and includes a binding pair comprising a first member and a second member, said first member being bound to the double-stranded DNA sequence, said second member being bound to the surface of the solid support.

13. **(Original)** The method according to claim 1, wherein the double-stranded DNA sequence(s) are covalently bound to the surface of the insoluble solid support.

14. **(Currently amended)** The method according to claim 1, wherein the double-stranded DNA ~~specific~~ sequence ~~is~~ comprises repeated specific sequences ~~on the same molecule~~.

15. **(Previously presented)** The method according to claim 1, wherein the double-stranded DNA sequences fixed on the support surface contain in part or totally one or several of the specific DNA sequences presented in the table 1.

16. **(Currently amended)** A screening and/or quantification method of one or more transcriptional factors(s) present in a cell or cell lysate, said method comprising the steps of:

~~a.~~ (a) binding to an insoluble solid support double-stranded DNA sequence(s) at the concentration of at least 0.01 pmole/cm^2 of said solid support surface, wherein the solid support is an array bearing at least 4 spots/cm^2 of solid support surface, each spot containing double-stranded DNA sequence(s) for the binding of transcriptional factor(s), said double-stranded DNA sequence comprising a specific sequence, said specific sequence being able to bind said one or more transcriptional factor(s) and said double-stranded DNA sequence being connected to the surface of the solid support by a

spacer wherein said spacer is ~~corresponding to or comprising at least~~ a double-stranded DNA nucleotide sequence of between about 50 and about 250 base pairs, or wherein the spacer comprises a double-stranded DNA nucleotide sequence of between about 50 and about 250 base pairs;

~~b.~~ (b) putting into contact said one or more transcriptional factor(s) with said bound double-stranded DNA sequence(s); and

~~c.~~ (c) identifying and/or quantifying a signal resulting from the binding of said transcriptional factor(s) upon said double-stranded DNA sequence(s),

wherein said transcriptional factor is the HIV integrase.

17. **(Currently amended)** The method according to claim 1, comprising the step of ~~identification of~~ identifying at least one characteristic specific of the transcriptional factor activation.

18. **(Original)** The method according to claim 1, which comprises the steps of screening, quantifying and/or recovering compounds able to bind to said transcriptional factor(s) or inhibit the binding of transcriptional factor(s) to the specific sequence upon the double-stranded DNA sequence(s) bound to said solid support.

19. **(Currently amended)** The method according to claim 1, which further comprises prior to step (b) the ~~steps~~ step of ~~screening, quantifying and/or recovering~~ contacting said cells with a candidate compound ~~compounds~~ which ~~modulate~~ is being evaluated to deterimine whether it modulates the binding and/or ~~the~~ activity of the said transcriptional factor(s) ~~when they are put in contact with cells, tissues or organisms~~.

20. **(Currently amended)** The method according to claim 1, which further comprises prior to step (b) the ~~steps~~ step of ~~screening, quantifying and/or recovering~~ contacting said cells with a candidate compound ~~compounds~~ which ~~modulate~~ is being evaluated to determine whether it modulates ~~the~~ activity of enzyme(s) or protein(s) acting on transcriptional factor(s)~~, and then assayed for the binding to and/or activity of said transcriptional factor(s)~~.

21. **(Currently amended)** A method according to claim 1, which further comprises the step of identifying ~~identification of~~ transcriptional factor(s) and/or ~~of~~ peptides which are part of ~~their~~ the transcriptional factor(s) active complex.

22. **(Currently amended)** The method according to claim 1, which comprises the step of adding in the cell lysate an externally added transcriptional factor or a compound which is able to bind to the ~~consensus~~ specific sequence.

23-33. **Cancelled**

34. **(Previously presented)** The method of Claim 12, wherein said binding pair is biotin/streptavidin.

35. **Cancelled**

36. **(Previously presented)** The method according to claim 12, wherein the binding pair is selected from the group consisting of biotin/streptavidin, hapten/receptor and antigen/antibody binding pair.

37. **(Previously presented)** The method according to claim 1, wherein step b) comprises putting into contact said one or more transcriptional factor(s) in a cell lysate with said bound double-stranded DNA sequence(s).

38. **Cancelled**

REMARKS

The following addresses the substance of the Office Action.

Priority

The Examiner asserts that Applicant cannot rely upon its foreign priority because a translation of the foreign priority document has not been received. It is Applicants understanding that the priority document is in English. Applicants thank the Examiner for the teleconference with Applicants representatives on July 6, 2005 in which the Examiner agreed to review the priority document and to contact Applicants representatives prior to preparing any subsequent action in this application if the priority document is not in English.

Claim objections

Claims 1, 2, 4-8, 12-15, 17, 18, 22, 34, 36 and 37 have been objected to for being grammatically unclear for reciting the phrase "a non-radioactive resulting signal". Claim 4, which is the only claim reciting the objected phrase has now been amended to recite "a non-radioactive signal". Therefore, Claims 1, 2, 4-8, 12-15, 17, 18, 22, 34, 36 and 37 are now clear.

Claims 1, 2, 4-8, 12-18, 22, 34, 36 and 37 have been objected to for containing a period after each sub-step. Claims 1 and 16 which contain the periods after each substep have been amended accordingly.

Claims 19-21 have been objected to being drawn to a separate invention, which can not be practiced together with the elected invention. Claims 19-21 have been amended to further clarify their relationship to the invention of Claim 1.

Compliance with 35 USC §112

The Examiner has rejected Claims 1, 2, 4-8, 12-18, 22, 34, 36 and 37 under 35 USC §112, second paragraph as being indefinite. More specifically, Claims 1 and 16 were found indefinite for reciting the phrase "said double-stranded DNA sequence being connected to the surface of the solid support by a spacer *corresponding to* or comprising at least a double-stranded DNA nucleotide sequence" as it is unclear what the difference is inferred between "corresponding to" and "comprising". The independent Claims 1 and 16 have been amended to now recite "wherein said spacer is a double-stranded DNA nucleotide sequence of between about 50 and about 250 base pairs, or wherein the spacer comprises a double-stranded DNA nucleotide

sequence of between about 50 and about 250 base pairs". Therefore, Claims 1, 2, 4-8, 12-18, 22, 34, 36 and 37 are now definite.

Claim 14 was found indefinite for having insufficient antecedent basis for the phrases "the specific sequence" and "the same molecule". Claim 14 has been amended to now recite "wherein the double-stranded DNA sequence comprises repeated specific sequences". Therefore, Claim 14 is now definite.

Claim 22 was found indefinite for having insufficient antecedent basis for the phrase "the consensus sequence". Claim 22 has now been amended to recite "the specific sequence". Therefore Claim 22 is now definite.

Applicant has addressed all the rejections under 35 USC §112, second paragraph of Claims 1, 2, 4-8, 12-18, 22, 34, 36, and 37, which are now definite. Therefore, their rejection should be withdrawn.

Compliance with 35 USC §103

The Examiner has rejected Claims 1, 2, 4-8, 12-18, 22, 36 and 37 under 35 USC §103(a) as being allegedly unpatentable over Peterson et al (USP 5,563,036) in view of Heslot et al. (USP 6,342,353 having a 102(e) date of November 4, 1999) and Nerenberg et al. (US 2002/0015198 with priority date of September 20, 2000). More specifically, the Examiner has stated that it would have been obvious to a person with an ordinary skill in the art at the time the invention was made to modify the teachings of Peterson et al. with that of Heslot et al. and Nerenberg et al. to arrive at the claimed invention.

> The rule is that to establish a *prima facie* case of obviousness, the PTO must cite one or more references that provide some suggestion or motivation to modify the references to achieve the claimed invention, provide a reasonable expectation of success to achieve the claimed invention, and finally, the cited art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).
>
> Furthermore, "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

Here, the cited art either taken alone or in combination, fails to provide the required factors.

As correctly observed by the Examiner, Peterson et al. neither suggest nor mention the use of a spacer between about 50 and about 250 bp as recited in the independent Claim 1. As was described in the Inventor's Declaration submitted previously (October 2, 2004), use of spacers between about 50 and about 250 bp in length provides enhanced signal levels relative to the levels observed when the binding site is separated from the support by shorter sequences with a length similar to those described in Peterson. These enhanced signal levels are particularly important in the context of microarrays, in which the binding of multiple factors to their recognition sites is evaluated under uniform binding conditions which may be suboptimal for the binding of at least some of the factors. In such situations, it is desirable to enhance signal levels as much as possible since the suboptimal binding conditions may result in a lower degree of binding than would be observed under optimal conditions. In this regard, it is important to note that the methods of Peterson are performed on multiwell plates as opposed to the microarrays utilized in the present methods. Thus, use of 10 bp sequences before the binding site as disclosed in Peterson is insufficient for use in the context of microarrays.

As was stated in the Inventor's Declaration under 37 C.F.R. §1.132 submitted previously, spacers between about 50 bp and about 250 bp provide advantages in binding efficiency. As described in the Declaration, the inventors first performed quantitation of signals resulting from NF-kB binding to recognition sites linked to spacers of various sizes: from 6 bp (close to conditions used by Peterson et al., where the spacer was 8 bp long) to 100 bp. Signal strengths for NF-kB binding were maximum with a spacer of 100 bp.

As was described in the Declaration, similar experiments revealed that increasing spacer lengths increased signal intensities for 4 transcription factors, Elk-1, c-Myk, STAT1 and STAT3, in addition to NF-kB. In addition, as was described in the Declaration, it was possible to detect and quantify 5 different transcriptional factors with accuracy on a microarray under the same binding conditions. Furthermore, contrary to detection of NFκB factor which was still detectable with the use of a small spacer (6 bp), some factors were hardly detectable (STAT3), or not detected at all (Elk-1) with a small spacer. The inventors also found that the signals measured with spacers below about 50 bp may not increase linearly with the spacer size. Therefore, high variability in signal detection using short (6 bp) spacers is totally incompatible with the simultaneous analysis of more than one factor as claimed in the present invention. Because the

binding conditions would be uniform on the array, it is likely that the binding conditions (salt concentrations, temperature, etc.) would be less than optimal for each of transcription factors. In view of the suboptimal binding conditions, the optimal spacer size provides important advantages in detecting and quantifying transcription factor binding. The inventors showed in the Declaration that the signals for all the tested transcription factors when tested simultaneously on a single array were maximal when the spacers were between about 50 and 150 basepairs. Therefore, the spacers between about 50 and about 250 base pairs are not obvious in view of Peterson et al.

Heslot et al. (US Patent 6 342 353B1) describes the use of a spacer arm which could be a double-stranded DNA having a length between 100 and 500 bases. However, this US patent is related to a non-analogous field of technology which concerns identification of signatures corresponding to specific sequences of double-stranded nucleic acids by separating the two strands of a nucleic acid duplex each attached to a separate support by a spacer, and then measuring the force necessary to move apart the two supports.

Furthermore, the third paragraph of column 4 (lines 16 to 17) referred by the Examiner, states that nucleotide sequences linked to a slide via the molecular construct (spacer arm) have some freedom of movement but that the length of the spacer arm may be advantageously adjusted in relation to the spatial resolution of the system for locating the position of the beads. Heslot et al. does not teach or suggest to the person skilled in the art that this "freedom of movement" of double-stranded DNA nucleotide sequence used to improve the measurement of the separation forces needed to move apart the two strands of a DNA pair, will also improve the binding of transcriptional factors upon a specific sequence of the double-stranded DNA, in specific conditions, wherein the solid support is a micro-array. In particular, the previous Declaration by the inventor shows that a spacer of a specific length will allow firstly the improvement of detection of some specific transcriptional factors (some transcriptional factors were detected by the use of small spacers, while other transcriptional factors are not detected) and would also improve the high variability in signal detection observed upon micro-array. Such unexpected results are not resulting from a "possible freedom of movements" of the bound double-stranded DNA sequences, but from the binding characteristics of the transcriptional factors to these DNA sequences. Indeed, the specific length of the spacer is important for improving the detection due

to the possible interference obtained with the solid support surface which reduces the possible binding characteristics of these transcriptional factors to their corresponding sequences.

Nerenberg et al. (with priority date of September 20, 2000) is not prior art over the present application, which is entitled to the priority date of March 24, 2000. The Applicant will submit the certified translation of the priority document shortly to support such entitlement.

In conclusion, Peterson et al. and Heslot et al. failed to support *prima facie* case of obviousness. These references both fail because neither provides the requisite motivation to combine, the reasonable expectation of success, or teaches all the limitations of the claimed invention. Because of these deficiencies, Applicants submit that the PTO failed to articulate a *prima facie* case of obviousness, and as such, request that the present rejection of Claims 1, 2, 4-8, 12-18, 22, 36 and 37 should be withdrawn.

The Examiner has rejected Claim 34 under 35 USC §103(a) as being allegedly unpatentable over Peterson et al (USP 5,563,036) in view of Heslot et al. (USP 6,342,353 having a 102(e) date of November 4, 1999) and Nerenberg et al. (US 2002/0015198 with priority date of September 20, 2000) and further in view of Dattagupta et al. (USP 4,968,602). More specifically, the Examiner stated that it would have been obvious to a person with an ordinary skill in the art at the time the invention was made to modify the teachings of Peterson et al. with that of Heslot et al. and Nerenberg et al. to substitute the avidin with streptavidin of Dattagupta et al. to arrive at the claimed method involving streptavidin/biotin binding.

The non-obviousness of Claims 1 and 12, to which Claim 34 depends, over Peterson et al. and Heslot et al. and irrelevance of Nerenberg et al. is discussed above. Dattagupta et al. fails to cure the deficiencies of the primary references. Therefore, Claim 34 is non-obvious over the cited references and its rejection under 35 USC §103(a) should be withdrawn.

Double Patenting

The Patent Office rejected claims 1, 2, 4-8, 12-18, 22, 34, 36 and 37 on the grounds of obviousness-type double patenting over claims 1-21, 25 and 26 of copending Application No. 10/821,568. A terminal disclaimer may be used to overcome an obviousness-type double patenting rejection. Applicant will defer filing a terminal disclaimer until the rejected claims are otherwise indicated to be in condition for allowance.

CONCLUSION

For the foregoing reasons, it is respectfully submitted that the rejections set forth in the outstanding Office Action are inapplicable to the present claims. Accordingly, Applicants request the expeditious allowance of the pending claims.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call the undersigned at the below-given phone number, to discuss such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 6, 2005

By: Daniel Hart

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Customer No. 20,995
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